STN Search history

10799320srch2.trn \$%^STN;HighlightOn= ***;HighlightOff=*** ;

Connecting via Winsock to STN

welcome to STN International! Enter x:X

LOGINID: mmpws25

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

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Web Page for STN Seminar Schedule - N. America
NEWS
          JAN 08
                   CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS
                   CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS
          JAN 16
                   IPC version 2007.01 thesaurus available on STN
NEWS
          JAN 16
                   WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS
          JAN 16
          JAN 22
                   CA/CAplus updated with revised CAS roles
NEWS
       6
          JAN 22
JAN 29
                   CA/CAplus enhanced with patent applications from India
NEWS
                   PHAR reloaded with new search and display fields CAS Registry Number crossover limit increased to 300,000 in
NEWS
          JAN 29
NEWS
                   multiple databases
          FEB 15
                   PATDPASPC enhanced with Drug Approval numbers
NEWS 10
NEWS 11
          FEB 15
                   RUSSIAPAT enhanced with pre-1994 records
NEWS 12
          FEB 23
                   KOREAPAT enhanced with IPC 8 features and functionality
NEWS 13
          FEB 26
                   MEDLINE reloaded with enhancements
                   EMBASE enhanced with Clinical Trial Number field
NEWS 14
          FEB 26
          FEB 26
FEB 26
NEWS 15
                   TOXCENTER enhanced with reloaded MEDLINE
                   IFICDB/IFIPAT/IFIUDB reloaded with enhancements
CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases
NEWS 16
NEWS 17
          FEB 26
NEWS 18
          MAR 15
                   WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS 19
          MAR 16
                   CASREACT coverage extended
NEWS 20
          MAR 20
                   MARPAT now updated daily
          MAR 22
NEWS 21
                   LWPI reloaded
NEWS 22
          MAR 30
                   RDISCLOSURE reloaded with enhancements
NEWS 23
          APR 02
                   JICST-EPLUS removed from database clusters and STN
                   GENBANK reloaded and enhanced with Genome Project ID field
NEWS 24
          APR 30
          APR 30
APR 30
                   CHEMCATS enhanced with 1.2 million new records CA/CAplus enhanced with 1870-1889 U.S. patent records
NEWS 25
NEWS 26
NEWS 27
          APR 30
                   INPADOC replaced by INPADOCDB on STN
NEWS 28
          MAY 01
                   New CAS web site launched
NEWS 29
          MAY 08
                   CA/CAplus Indian patent publication number format defined
NEWS 30
          MAY 14
                   RDISCLOSURE on STN Easy enhanced with new search and display
                   fields
NEWS 31
          MAY 21
                   BIOSIS reloaded and enhanced with archival data
NEWS 32
          MAY 21
                   TOXCENTER enhanced with BIOSIS reload
NEWS 33
          MAY 21
                   CA/CAplus enhanced with additional kind codes for German
                   patents
NEWS 34
          MAY 22
                   CA/CAplus enhanced with IPC reclassification in Japanese
                   patents
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NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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NEWS LOGIN Welcome Banner and News Items
Page 1

NEWS IPC8 For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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=> f registry
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Some commands only work in certain files. For example, the EXPAND
command can only be used to look at the index in a file which has an
index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of
commands which can be used in this file.

=> file registry
COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 1.26 1.26

FULL ESTIMATED COST

FILE 'REGISTRY' ENTERED AT 15:43:33 ON 11 JUN 2007 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2007 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 10 JUN 2007 HIGHEST RN 936909-28-3 DICTIONARY FILE UPDATES: 10 JUN 2007 HIGHEST RN 936909-28-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> expand paroxetine

ENTER FIELD CODE (BI):cn **E**1 PAROXAZINE/CN E2 1 PAROXET/CN E3 1 --> PAROXETINE/CN **E4** 1 PAROXETINE ACETATE/CN E5 1 PAROXETINE DIHYDROGEN PHOSPHATE/CN E6 1 PAROXETINE FORMATE/CN 1 PAROXETINE GLYCYRRHIZINATE/CN E7 PAROXETINE HYDROBROMIDE/CN E8 1 E9 PAROXETINE HYDROCHLORIDE/CN Page 2

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E10
E11
                      PAROXETINE HYDROCHLORIDE ISOPROPANOLATE/CN
               1
E12
                      PAROXETINE HYDROGEN PHOSPHATE/CN
=> s e3
               1 PAROXETINE/CN
L1
=> d 11 1
L1
     ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS ON STN
RN
     61869-08-7 REGISTRY
                     16 Nov 1984
ED
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      (3s, 4r) -
                 (CA INDEX NAME)
OTHER CA INDEX NAMES:
      Piperidine, 3-[(1,3-benzodioxol-5-yloxy)methyll-4-(4-fluorophenyl)-.
      (3S-trans)-
OTHER NAMES:
      (-)-Paroxetine
CN
      (-)-trans-4-(4-Fluorophenyl)-3-(3,4-methylenedioxyphenoxymethyl)piperidine
CN
CN
     Aropax
CN
     Besitram
     BRL 29060
CN
CN
     Casbol
     FG 7051
CN
CN
     Frosinor
CN
     Motivan '
        ***Paroxetine***
CN
CN
     Paxetil
CN
     Paxil
     PaxPar
CN
FS
     STEREOSEARCH
     63952-24-9
DR
MF
     C19 H20 F N O3
CI
     COM
        N Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, DDFU,
       DRUGU, EMBASE, IMSDRUGNEWS; IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, ULIDAT, USAN, USPATZ, USPATFULL
          (*File contains numerically searchable property data)
     Other Sources:
                         WHO
Absolute stereochemistry. Rotation (-).
/ Structure 1 in file .gra /
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**
              2336 REFERENCES IN FILE CA (1907 TO DATE)
                40 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
             2346 REFERENCES IN FILE CAPLUS (1907 TO DATE)
=> d 11 1 all
     ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN
L1
                   REGISTRY
     61869-08-7
RN
     Entered STN: 16 Nov 1984
ED
     Piperidine, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-, (3S,4R)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
                                             Page 3
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10799320srch2.trn
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CN
      (3S-trans)-
OTHER NAMES:
CN
      (-)-Paroxetine
      (-)-trans-4-(4-Fluorophenyl)-3-(3,4-methylenedioxyphenoxymethyl)piperidine
CN
CN
CN
      Besitram
      BRL 29060
CN
CN
      Casbol
      FG 7051
CN
CN
      Frosinor
CN
      Motivan
         ***Paroxetine***
CN
      Paxetil
CN
CN
      Paxil
      PaxPar
CN
FS
      STEREOSEARCH
      63952-24-9
DR
      C19 H20 F N O3
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CI
      COM
LC
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        DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE,
        MRCK*, PHAR, PROMT, PROUSDOR, PS, RTECS*, SYNTHLINE, TOXCENTER, ULIDAT,
               USPAT2, USPATFULL
           (*File contains numerically searchable property data)
      Other Sources:
                          WHO
        CAplus document type: Book; Conference; Dissertation; Journal; Patent;
DT.CA
        Report
RL.P
        Roles from patents: ANST (Analytical study); BIOL (Biological study);
        FORM (Formation, nonpreparative); PREP (Preparation); PROC (Process);
        PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P
        Roles for non-specific derivatives from patents: ANST (Analytical
        study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP
        (Properties); RACT (Reactant or reagent); USES (Uses)
Roles from non-patents: ANST (Analytical study); BIOL (Biological
RL.NP
study); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical
        study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES
        (Uses)
Ring System Data
Elemental|Elemental| Size of |Ring System|
                                                     Ring
                                                                  RID
Analysis
           Sequence
                       |the Rings|
                                      Formula
                                                 |Identifier|Occurrence
   EA
               ES
                           57
                                        RF
                                                     RID
                                                                 Count
C6
           C6
                       6
                                   C6
                                                 |46.150.18 |1
C5N
           NC5
                                   C5N
                                                  46.156.1
C302-C6
           lococ2-c6 15-6
                                   C702
                                                 |333.584.8 |1
Absolute stereochemistry. Rotation (-).
/ Structure 2 in file .gra /
Experimental Properties (EPROP)
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CONDITION

Page 4

NOTE

PROPERTY (CODE)

| VALUE |

=======	=======	=====	⊦== ==	====	-===	=====	=======	:+====	====
	Rotatory	Power	-66					(1)	CAS
(ORP)			l		Solv:	metha	anol	ì	
					(67-5		•	İ	
			l		Temp:	20 de	eq C		
			ĺ		Wavle			İ	

(1) Segura, Mireia; Bioorganic Chemistry 2003 V31(3) P248-258 CAPLUS Experimental Property Tags (ETAG)

PROPERTY	ן אס	ĻΕ
Acid/Base Dissociation Constant (Ka/Kb) 1 more tag shown in the MAX or ETAGFULL formats	 (1)	CAS
ADME (Absorption, Distribution, Metabolism, Excretion) 2 more tags shown in the MAX or ETAGFULL formats	(2)	CAS
Carbon-13 NMR Špectra IR Spectra		CAS CAS
1 more tag shown in the MAX or ETAGFULL formats Mass Spectra 10 more tags shown in the MAX or ETAGFULL formats	(5)	CAS
Proton NMR Spectra 1 more tag shown in the MAX or ETAGFULL formats	(3)	CAS
Solubility UV and Visible Absorption Spectra Vapor Pressure/Volatility		CAS CAS CAS

- (1) Vasskog, Terje; Journal of Chromatography, A 2006 V1115(1-2) P187-195
- Grasmaeder, Katja; European Journal of Clinical Pharmacology 2004 V60(5) P329-336 CAPLUS Segura, Mireia; Bioorganic Chemistry 2003 V31(3) P248-258 CAPLUS Sugi, Kiyoshi; EP 1384711 A1 2004 CAPLUS Thieme, Detlef; Analytica Chimica Acta 2003 V492(1-2) P171-186 CAPLUS Cunningham, Virginia L.; Environmental Science and Technology 2004 V38(12) P3351-3359 CAPLUS (2)

- (3) (4) (5)

Predicted Properties (PPROP)

PROPERTY (CODE)	VALUE	CONDITION	NOTE
Boiling Point (BP) Density (DEN) Enthalpy of Vap. (HVAP)	11.0 11.0 11.0 11.0 11.0 11.0 12.98 124.90 173.46 451.7+/-45.0 deg C 11.213+/-0.06 g/cm**3 171.08+/-3.0 kJ/mol 1227.0+/-28.7 deg C 4	PH 1	
Koc (KOC)	2.47 Page 5	рн 1 25 deg C	j (1)

	10799320srch2.trn	•	
logD (LOGD) logD (LOGD) logD (LOGD) logD (LOGD) logD (LOGD) logD (LOGD) logP (LOGP)	2.47 2.47 2.48 2.49 2.62 3.97 17.39 145.43 1013.29 0.79 0.79 0.79 0.79 0.79 0.79 0.79 0.79 1.00 1.64 2.56 3.40 3.890+/-0.436 0.0099 g/L	рн 3 25 deg C	
Mass Solubility (SLB.MASS) Mass Solubility (SLB.MASS) Mass Solubility (SLB.MASS) Mass Solubility (SLB.MASS) Mass Solubility (SLB.MASS) Mass Solubility (SLB.MASS) Mass Solubility (SLB.MASS) Mass Solubility (SLB.MASS) Mass Solubility (SLB.MASS) Mass Solubility (SLB.MASS) Mass Solubility (SLB.MASS) Mass Solubility (SLB.MASS) Mass Solubility (SLB.MASS)	13 g/L 13 g/L 13 g/L 12 g/L 12 g/L 12 g/L 17.6 g/L 1.7 g/L 0.21 g/L 0.030 g/L 0.040 g/L	pH 4 25 deg C pH 5 25 deg C pH 6 25 deg C pH 7 25 deg C pH 8 25 deg C	
(ISLB.MOL) Molar Solubility (SLB.MOL)	 0.038 mol/L 0.038 mol/L 0.037 mol/L 0.037 mol/L 0.035 mol/L 0.023 mol/L 0.0053 mol/L 0.00064 mol/L 0.000092 mol/L 0.00012 mol/L	ph 1 25 deg C ph 2 25 deg C ph 3 25 deg C ph 4 25 deg C ph 5 25 deg C ph 6 25 deg C ph 7 25 deg C ph 8 25 deg C ph 9 25 deg C ph 10 25 deg C Unbuffered Water ph 9.85 25 deg C	
Molecular Weight (MW) pKa (PKA) Polar Surface Area (PSA)	329.37 10.32+/-0.60 39.72 A**2	Most Basic 25 deg C	(1) (1) (1)
Vapor Pressure (VP)	2.39E-08 Torr	25 deg C	(1)

(1) Calculated using Advanced Chemistry Development (ACD/Labs) Software V8.14 ((C) 1994-2007 ACD/Labs)

See HELP PROPERTIES for information about property data sources in REGISTRY. Page $\,6\,$

2336 REFERENCES IN FILE CA (1907 TO DATE)
40 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2346 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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REFERENCE 1
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146:507832 CA <<LOGINID::20070611>>
ΑN
         Multi-stage process to control particle size of pharmaceutical substance
TI
IN
         Mooney, Brett Antony
         Alphapharm Pty. Ltd., Australia; Keramidas, Panagiotis
PA
S0
         PCT Int. Appl., 27pp.
         CODEN: PIXXD2
DT
         Patent
LA
         English
         63-8 (Pharmaceuticals)
CC
FAN.CNT 1
                                                                                APPLICATION NO.
         PATENT NO.
                                         KIND DATE
         wo 2007053904
                                                    20070518
PΙ
                                          Α1
                                                                                WO 2006-AU1687
                                                                                                                20061110
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                        CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
                        GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN,
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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, IS, MW, MZ, NA, SD, SI, SZ, TZ, UG, ZM, ZW, AM, AZ, RY
                        GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
                        KG, KZ, MD, RU, TJ, TM
PRAI AU 2005-906227
                                         20051110
         This invention relates to multi-stage process to control the particle size
        of a pharmaceutical substance comprising the steps of: passing the pharmaceutical substance through a first stage of a particle size redn. process with a first set of particle size control parameters to obtain a feedstock of reduced median particle size and lesser distribution of median particle size for a second stage of a particle size redn. process; passing the feedstock, through a second stage of a particle size redn. process with a second set of particle size control parameters; optionally, using the product of the second stage or subsequent stages as a feedstock
         using the product of the second stage or subsequent stages as a feedstock
         in further stages of a multi-stage particle size redn. process with a set of particle size control parameters for each stage; and collecting a
         pharmaceutical substance with a median particle size greater than 10.mu.m and with a narrow, reproducible distribution of median particle sizes. Thus, oxcarbazepine was milled in a 12" spiral jet mill to produce particle size of 15.mu.m to 17.mu.m.
ST
         milling particle size drug
         Schizophrenia
IT
               (anti-schizophrenic agent; multi-stage process to control particle size
               of pharmaceutical substance)
         Milling (size reduction)
(jet; multi-stage process to control particle size of pharmaceutical
IT
               substance)
       Angiotensin receptor antagonists
         Anticholesteremic agents
         Anticonvulsants
         Antidepressants
         Antidiabetic agents
         Antihypertensives
         Antimalarials
         Milling (size reduction)
         Particle size
```

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(multi-stage process to control particle size of pharmaceutical substance)

IT Transport proteins

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(multi-stage process to control particle size of pharmaceutical

substance)

IT

- 50-52-2, Thioridazine 50-53-3, Chlorpromazine, biological studies 52-53-9, Verapamil 52-86-8, Haloperidol 54-31-9, Frusemide 63-42-3, 86-54-4, Hydralazine 113-45-1, Methylphenidate 131-01-1. 298-46-4, Carbamazepine 500-92-5, Proguanil 525-66-6 2709-56-0, Flupenthixol 5786-9003-39-8, Polyvinylpyrrolidone 548-73-2, Droperidol Propranolol 5786-21-0, 6452-71-7, Oxprenolol Clozapine 9004-32-4, Sodium carboxymethyl cellulose 9004-34-6D, Cellulose, deriv. 9004-64-2, Hydroxypropyl cellulose ulose 13523-86-9, Pindolol 1480 9004-62-0, Hydroxyethyl cellulose 9004-65-3, Hydroxypropyl methylcellulose 3 -6, Talc, biological studies 21829-25-4, M Gemfibrozil 28721-07-5, Oxcarbazepine 29 7, Diltiazem 49562-28-9, Fenofibrate 509 -1, Metoprolol 53772-83-1, Zuclopenthixol 14807-96 21829-25-4, Nifedipine 25812-3 bazepine 29122-68-7, Atenolol 25812-30-0. 42399-41-50925-79-6, Colestipol 51 ol 54910-89-3, Fluoxetine 51384-51 60142-96-3, Gabapentin 61869-08-7, Paroxetine 59729-33-8, Citalopram 71675-85-9, Amisulpride 74772-77-3, Ciglitazone 66722-44-9, Bisoprolol 62571-86-2, Captopril 72956-09-3, Carvedilol 73590-58-6, Omeprazole 75847-73-3, Enalapril 76547-98-3, Lisinopril 79617-96-2, Sertraline 81093-37-0, Pravastatin 79902-63-9, Simvastatin Perindopril 83015-26-3 82834-16-0, Perindopril 83015-26-3, Atomoxetine 85441-61-8, Mirtazapine 87333-19-5, Ramipril 87679-37-6, -8, Desvenlafaxine 93413-69-5, Venlafaxine 9395233-18-4, Atovaquone 97322-87-7, Troglitazone 85441-61-8, Quinapril 87679-37-6, Trandolapril 85650-52-8 87679-37-6. 93413-62 93957-54-1, Fluvastatin one 102625-70-7, 103577-45-3, Lansoprazole 111025-46-8, Pioglitazone Pantoprazole 114798-26-4, Losartan 115103-54-3, Tiag 119141-88-7, Esomeprazole 122320-73-4, 115103-54-3, Tiagabine 111974-69-7, Quetiapine 117976-89-3, Rabeprazole 129722-12-9, Aripiprazole 128196-01-0, Escitalopram Rosiglitazone 133040-01-4, Eprosartan 132539-06-1, Olanzapine 134523-00-5, 135062-02-1, Repaglinide 137862-9 tan 139481-59-7, Candesartan 1447 Pregabalin 163222-33-1, Ezetimibe NVP DPP728 251572-86-8, P32/98 27 137862-53-4, Valsartan Atorvastatin 138402-11-6, Irbesartan 13948 148553-50-8, Pregabalin 247016-69-9, NVP DPP728 361442-04-8, Saxagliptin 144701-48-4, Telmisartan be 171092-64-1, FE 999011 274901-16-5, Vildagliptin 486460-32-6, Sitagliptin 898546-83-3. PHX RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
 - (Uses)
 (multi-stage process to control particle size of pharmaceutical

substance)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

(1) Ranbaxy Laboratories Limited; WO 2006030301 A 2006 CAPLUS

(2) Tomoaki, H; US 6383520 B CAPLUS

(3) Verheezen, J; International Journal of Pharmaceutics 2004, V278(1), P165 CAPLUS

REFERENCE 2

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AN 146:501032 CA <<LOGINID::20070611>>
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- TI Process for preparing paroxetine hydrochloride hemihydrate
- IN Dubey, Shailendra Kumar; Kumar, Pramod; Dubey, Sushil Kumar
- PA Jubilant Organosys Ltd., India
- SO PCT Int. Appl., 17pp.

CODEN: PIXXD2

- DT Patent
- LA English
- CC 28-5 (Heterocyclic Compounds (More Than One Hetero Atom))
 Section cross-reference(s): 45

FAN.CNT 1

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10799320srch2.trn
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PATENT NO.
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                                     DATE
                                                         APPLICATION NO.
                                                                               DATE
      wo 2007054978
                                                                               20061110
PΙ
                                     20070518
                                                        WO 2006-IN446
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                 CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
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KG, KZ, MD, RU, TJ, TM
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      A process for the prepn. of cryst. paroxetine hydrochloride in hemihydrate form employing a selective solvent system to achieve stable and non-hygroscopic form which is easy to prep. and convenient to operate on
      com. scale is described. The process comprises crystg. paroxetine
      hydrochloride using an alc. solvent, such as methanol, ethanol,
      n-propanol, isopropanol or their mixt. and isolating the crystd. product
      by optionally adding secondary solvent, such as diisopropyl ether or Me
      tert-Bu ether
ST
      paroxetine hydrochloride hemihydrate prepn solvent
IT
      Alcohols, uses
      Aromatic hydrocarbons, uses
      Esters, uses
      Ethers, uses
      RL: NUU (Other use, unclassified); USES (Uses)
           (solvent system for prepn. of paroxetine hydrochloride hemihydrate)
      110429-35-1P, Paroxetine hydrochloride hemihydrate
IT
      RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP
      (Preparation)
           (solvent system for prepn. of paroxetine hydrochloride hemihydrate)
               67-66-3, Chloroform, uses 71-23-8, n-Propanol, uses 75-09-2, comethane, uses 108-20-3, Diisopropyl ether 108-88-3, Toluene,
IT
      64-17-5, Ethanol, uses
      Dichloromethane, uses 108-20-3, Diisopropyl ether 108-88-3, Toluenouses 141-78-6, Ethyl acetate, uses 1634-04-4
RL: NUU (Other use, unclassified); USES (Uses)

(solvent system for prepn. of paroxetine hydrochloride hemihydrate)
                                       78246-49-8, Paroxetine hydrochloride
IT
      61869-08-7, Paroxetine
      RL: RCT (Reactant); RACT (Reactant or reagent) (solvent system for prepn. of paroxetine hydrochloride hemihydrate)
REFERENCE 3
      146:501030 CA <<LOGINID::20070611>>
      Process for resolution and producing paroxetine salts and their hydrates
TI
      Kreidl, Janos; Czibula, Laszlo; Nemes, Andras; Harsanyi, Kalman;
      Deutschne, Juhasz Ida; Csutoras, Laszlo; Werkne, Papp Eva; Nagyne, Bagdy
      Judit; Borza, Istvan; Hegedues, Istvan
PΑ
      Richter Gedeon Vegyeszeti Gyar Rt., Hung.
SO
      Hung. Pat. Appl., 25pp.
      CODEN: HUXXCV
DT
      Patent
      Hungarian
LA
IC
      ICM C07D405-12
      28-5 (Heterocyclic Compounds (More Than One Hetero Atom))
      Section cross-reference(s): 22
FAN.CNT 1
      PATENT NO.
                             KIND DATE
                                                        APPLICATION NO.
                                                                              DATE
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19980928 PΙ ни 9601858 Α2 ни 1996-1858 19960708 20000628 HU 9601858 Α3 HU 221922 20030228 в1 PRAI HU 1996-1858 19960708

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

The invention concerns a process for the prepn. of paroxetine, its salts and hydrates of the formula I.HCl by (a1) reacting a novel cis, trans, racemic or optically active II (X = H, halogen, R-SO3-; where R = substituted alkyl or aryl group) with sesamol to obtain the trans compd. III that can be racemic or optically active; (a2) catalytic debenzylation of compd. III or its acid addn. salts; (a3) sepn. of the obtained I compd., its salts or hydrates; (a4) solvation of I; (a5) deliberating the base from the optically active salt, or forming the hydrochloride hemihydrate. According to an alternative (b) a trans compd. of III that can be racemic or optically active or is an acid addn. salt (b1) is catalytically de-benzylated; (b2) the obtained I compd., its salts or hydrates are sepd.; (b3) I is resolved; (b4) the base is deliberated from the optically active salt, or the hydrochloride hemihydrate is formed.

resoln paroxetine hydrate prepn ST

IT Resolution (separation)

(process for resoln. and producing paroxetine salts and their hydrates) 61869-08-7P, Paroxetine 78246-49-8P 105813-13-6P 105813-14-7P RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP IT (Preparation)

(process for resoln. and producing paroxetine salts and their hydrates) -31-3, Sesamol 5137-55-3, Tricaprylmethylammonium chloride 201855-6 201855-69-8 201855-71-2 201855-74-5 201855-75-6 533-31-3, Sesamol IT 6-5 RL: RCT (Reactant); RACT (Reactant or reagent)

(process for resoln. and producing paroxetine salts and their hydrates)

IT 201855-76-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for resoln. and producing paroxetine salts and their hydrates)

REFERENCE 4

146:498634 CA <<LOGINID::20070611>> AN

Prediction of treatment response by HPA-axis and glucocorticoid receptor polymorphisms in major depression TI

Brouwer, Jantien P.; Appelhof, Bente C.; van Rossum, Elisabeth F. C.; Koper, Jan W.; Fliers, Eric; Huyser, Jochanan; Schene, Aart H.; Tijssen, Jan G. P.; Van Dyck, Richard; Lamberts, Steven W. J.; Wiersinga, Wilmar ΑU M.; Hoogendijk, Witte J. G.

Department of Endocrinology, Academic Medical Center, Amsterdam, 1105 AZ, CS

SO Psychoneuroendocrinology (2006), 31(10), 1154-1163 CODEN: PSYCDE; ISSN: 0306-4530

PB Elsevier Ltd.

DT Journal

English LA

CC 14-10 (Mammalian Pathological Biochemistry)

Section cross-reference(s): 2, 3

Objective: We investigated whether treatment response is predicted by AB hypothalamus-pituitary-adrenal (HPA) axis parameters, or by genetic polymorphisms in the glucocorticoid receptor (GR), that regulates its feedback. Methods: Ninety-eight outpatients completed 8 wk of paroxetine treatment. Treatment response was defined as a 50% decrease in Hamilton Page 10

Rating Scale for depression (HRSD) ratings. At baseline, 24 h urinary cortisol excretion, and cortisol and ACTH concns. in a DEX/CRH test were The presence of polymorphisms in the GR DNA sequence (BclI, ER22/23EK, N363S) was detd. Prediction of treatment response was analyzed by calcg. response rates per tertile of an HPA-axis parameter and per GR genotype. Results: The response rate in the high ACTH tertile was significantly lower as compared to the intermediate tertile, but not compared to the low tertile (response rates from high to low tertile: 33%, 67% and 42%). Carriers of the BclI polymorphism had higher ACTH values than non-carriers (baseline ACTH: 3 vs. 5 ng/l, p=0.02) and showed a trend towards lower decrease of HRSD rates than non-carriers (HRSD decrease: 8 vs. 11, resp., p=0.07). In a subgroup of BclI carriers, patients in the high ACTH tertile had a lower decrease in HRSD and lower response rates than patients in the low ACTH tertiles (HRSD decrease from high to low tertile: 5, 9 and 11, p < 0.01). Conclusion: The results suggest that hyperactivity of the HPA-axis predict worse treatment outcome. The BclI $\,$ polymorphism explains, in part, DEX/CRH test results and tends to be assocd. with worse treatment outcome.

ST hypothalamus pituitary adrenal axis glucocorticoid receptor gene polymorphism depression

IT 5-HT reuptake inhibitors

Adrenal gland

Genetic polymorphism

Genotypes

Human

Pituitary gland

(DEX/CRH test show high ACTH and trend towards lower decrease of HRSD rate in patient with depression carrying Bcl1 polymorphism than non-carrier suggest hyperactivity of hypothalamus-pituitary-adrenal axis predict worse treatment outcome)

Gene, animal IT

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(GR; prediction of treatment response by HPA-axis and glucocorticoid receptor polymorphisms in major depression)

IT Endocrine system

(adrenal-hypothalamus-pituitary; DEX/CRH test show high ACTH and trend towards lower decrease of HRSD rate in patient with depression carrying Bcll polymorphism than non-carrier suggest hyperactivity of

hypothalamus-pituitary-adrenal axis predict worse treatment outcome)

Mental and behavioral disorders

(depression; DEX/CRH test show high ACTH and trend towards lower decrease of HRSD rate in patient with depression carrying Bcll polymorphism than non-carrier suggest hyperactivity of hypothalamus-pituitary-adrenal axis predict worse treatment outcome)

IT Brain

IT

IT

(hypothalamus; DEX/CRH test show high ACTH and trend towards lower decrease of HRSD rate in patient with depression carrying Bcl1 polymorphism than non-carrier suggest hyperactivity of

hypothalamus-pituitary-adrenal axis predict worse treatment outcome)

Glucocorticoid receptors IT

> RL:_ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)

(prediction of treatment response by HPA-axis and glucocorticoid

receptor polymorphisms in major depression)

50-23-7, Cortisol 9002-60-2, Adrenocorticotropic hormone, biological studies

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)

(DEX/CRH test show high ACTH and trend towards lower decrease of HRSD rate in patient with depression carrying Bcll polymorphism than non-carrier suggest hyperactivity of hypothalamus-pituitary-adrenal axis predict worse treatment outcome)

Page 11

50-02-2, Dexamethasone IT 12794-10-4, Benzodiazepine RL: BSU (Biological study, unclassified); BIOL (Biological study)
(DEX/CRH test show high ACTH and trend towards lower decrease of HRSD rate in patient with depression carrying Bcl1 polymorphism than non-carrier suggest hyperactivity of hypothalamus-pituitary-adrenal axis predict worse treatment outcome) 61869-08-7, Paroxetine IT RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (DEX/CRH test show high ACTH and trend towards lower decrease of HRSD rate in patient with depression carrying Bcl1 polymorphism than non-carrier suggest hyperactivity of hypothalamus-pituitary-adrenal axis predict worse treatment outcome) THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD 23 RE.CNT (1) American Psychiatric Association; Diagnostic and statistical manual of mental disorders, DSM-IV, 4th ed 1994
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with placebo or fixed-dose venlafaxine ER (75 mg/day or 150 mg/day), or Page 12

paroxetine 40 mg/day. The primary measure was the percentage of patients free from full-symptom panic attacks, assessed with the Panic and Anticipatory Anxiety Scale (PAAS). Secondary measures included the Panic Disorder Severity Scale, Clin. Global Impressions-Severity (CGI-S) and - Improvement (CGI-I) scales; response (CGI-I rating of very much improved or much improved), remission (CGI-S rating of not at all ill or borderline ill and no PAAS full-symptom panic attacks); and measures of depression, anxiety, phobic fear and avoidance, anticipatory anxiety, functioning, and quality of life.

panic disorder venlafaxine paroxetine depression anxiety antidepressant ST

IT Mental and behavioral disorders

(depression; venlafaxine extended-release and paroxetine were effective and well tolerated in treatment of depression patient)

IT **Emotion**

(fear; venlafaxine extended-release and paroxetine were effective and well tolerated to improve fear in treatment of patient with anxiety)

IT Anxiety

(panic disorder; venlafaxine extended-release and paroxetine were effective and well tolerated in treatment of panic disorder patient)

IT 5-HT reuptake inhibitors

(selective serotonin reuptake inhibitor paroxetine was effective and well tolerated in treatment of panic disorder patient)

Serotonin-noradrenaline reuptake inhibitors TT

(serotonin-norepinephrine reuptake inhibitor venlafaxine extended-release was effective and well tolerated in treatment of panic disorder patient)

Drug delivery systems ΙT

(tablets, sustained-release; venlafaxine extended-release and paroxetine were effective and well tolerated in treatment of panic disorder patient)

Antidepressants TT

(venlafaxine extended-release and paroxetine were effective and well tolerated in treatment of depression patient)

TT

(venlafaxine extended-release and paroxetine were effective and well tolerated in treatment of panic disorder patient)

IT Anxiety

> (venlafaxine extended-release and paroxetine were effective and well tolerated in treatment of patient with anxiety)

IT 61869-08-7, Paroxetine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(paroxetine was effective and well tolerated in treatment of panic disorder patient)

IT 93413-69-5, Venlafaxine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(venlafaxine extended-release was effective and well tolerated in treatment of panic disorder patient)

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146:493265 CA <<LOGINID::20070611>> TI

Selective Serotonin Reuptake Inhibitors, Fluoxetine and Paroxetine, Attenuate the Expression of the Established Behavioral Sensitization Induced by Methamphetamine

ΑU Kaneko, Yujiro; Kashiwa, Atsushi; Ito, Takashi; Ishii, Sumikazu; Umino, Asami; Nishikawa, Toru

CS Section of Psychiatry and Behavioral Sciences, Tokyo Medical and Dental Page 14

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Neuropsychopharmacology (2007), 32(3), 658-664 SO

CODEN: NEROEW; ISSN: 0893-133X

Nature Publishing Group PB DT Journal

English LA

1-11 (Pharmacology) CC

To obtain an insight into the development of a new pharmacotherapy that AB prevents the treatment-resistant relapse of psychostimulant-induced psychosis and schizophrenia, we have investigated in the mouse the effects of selective serotonin reuptake inhibitors (SSRI), fluoxetine (FLX) and paroxetine (PRX), on the established sensitization induced by methamphetamine (MAP), a model of the relapse of these psychoses, because the modifications of the brain serotonergic transmission have been reported to antagonize the sensitization phenomenon. In agreement with previous reports, repeated MAP treatment (1.0 mg/kg a day, s.c. (s.c.)) for 10 days induced a long-lasting enhancement of the increasing effects of a challenge dose of MAP (0.24 mg/kg, s.c.) on motor activity on day 12 or 29 of withdrawal. The daily injection of FLX (10 mg/kg, s.c.) or PRX (8 mg/kg, s.c.) from 12 to 16 days of withdrawal of repeated MAP administration markedly attenuated the ability of the MAP pretreatment to augment the motor responses to the challenge dose of the stimulant 13 days after the SSRI injection. The repeated treatment with FLX or PRX alone failed to affect the motor stimulation following the challenge of saline and MAP 13 days later. These results suggest that the intermittent and repetitive elevation of serotonergic tone may inhibit the expression of the motor sensitization induced by pretreatment with MAP. It is proposed It is proposed that clin. available serotonin reuptake inhibitors could be useful for preventing the recurrence of hallucinatory-paranoid state in drug-induced psychosis and schizophrenia.

selective serotonin reuptake inhibitor fluoxetine paroxetine ST methamphetamine behavioral sensitization; psychostimulant schizophrenia

psychosis

IT Behavior

IT

(motor; selective serotonin reuptake inhibitors fluoxetine and paroxetine attenuated methamphetamine-induced motor activity in mouse) Mental and behavioral disorders

(psychosis; selective serotonin reuptake inhibitors can be useful for prevention of hallucinatory-paranoid state in drug induced psychosis)

IT Schizophrenia

> (selective serotonin reuptake inhibitors can be useful for prevention of hallucinatory-paranoid state in drug induced schizophrenia)

5-HT reuptake inhibitors TT

Drugs of abuse

Human

Prophylaxis

Psychostimulants

(selective serotonin reuptake inhibitors fluoxetine and paroxetine attenuated expression of established behavioral sensitization induced by methamphetamine in mouse)

IT Behavior

> (sensitization; selective serotonin reuptake inhibitors fluoxetine and paroxetine attenuated expression of established behavioral sensitization induced by methamphetamine in mouse)

54910-89-3, Fluoxetine IT

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(selective serotonin reuptake inhibitor fluoxetine attenuated expression of established behavioral sensitization induced by methamphetamine in mouse)

61869-08-7, Paroxetine IT

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(selective serotonin reuptake inhibitor paroxetine attenuated expression of established behavioral sensitization induced by methamphetamine in mouse)

IT

537-46-2, Methamphetamine RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); BIOL (Biological study)

(selective serotonin reuptake inhibitors fluoxetine and paroxetine attenuated expression of established behavioral sensitization induced by methamphetamine in mouse)

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146:493256 CA <<LOGINID::20070611>>

Phencyclidine-Induced Cognitive Deficits in Mice are Improved by TI Subsequent Subchronic Administration of Fluvoxamine: role of Sigma-1

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Hashimoto, Kenji; Fujita, Yuko; Iyo, Masaomi ΑU

Division of Clinical Neuroscience, Chiba University Center for Forensic CS Mental Health, Chiba, Japan

Neuropsychopharmacology (2007), 32(3), 514-521 SO CODEN: NEROEW; ISSN: 0893-133X

Nature Publishing Group

PB DT Journal

English LA CC

1-11 (Pharmacology) AB This study was undertaken to examine the effects of the selective serotonin reuptake inhibitors fluvoxamine and paroxetine on cognitive deficits in mice after repeated administration of the N-methyl-D-aspartate receptor antagonist phencyclidine (PCP). In the novel object recognition test, repeated administration of PCP (10 mg/kg/day, 10 days) significantly decreased the exploratory preference in the retention test session, but not in the training test session. PCP-induced cognitive deficits were significantly improved by subsequent subchronic (2-wk) administration of fluvoxamine (20 mg/kg/day), but not paroxetine (10 mg/kg/day). Furthermore, the effect of fluvoxamine on PCP-induced cognitive deficits was antagonized by co-administration of the selective sigma-1 receptor antagonist NE-100 (1 mg/kg/day). Moreover, PCP-induced cognitive deficits were also significantly improved by subsequent subchronic (2-wk) administration of the selective sigma-1 receptor agonist SA4503 (1 mg/kg/day) or neurosteroid dehydroepiandrosterone 3-sulfate (DHEA-S; 25 mg/kg/day). The effects of SA4503 or DHEA-S were also antagonized by co-administration of NE-100 (1 mg/kg/day), suggesting the role of sigma-1 receptors in the active mechanisms of these drugs. In contrast, acute single administration of these drugs (fluvoxamine, paroxetine, SA4503) alone or combination with NE-100 did not alter PCP-induced cognitive The present study suggests that agonistic activity of deficits. fluvoxamine at sigma-1 receptors plays a role in the active mechanisms of fluvoxamine on PCP-induced cognitive deficits in mice. Therefore, sigma-1 receptor agonists such as fluvoxamine would be potential therapeutic drugs for the treatment of the cognitive deficits of schizophrenia. ST

phencyclidine cognitive deficit schizophrenia sigma I receptor fluvoxamine

paroxetine

IT Glutamate receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NMDA-binding, antagonist; cognitive deficits induced by phencyclidine were improved by fluvoxamine but not by paroxetine in mouse)

5-HT reuptake inhibitors

Cognition

IT

IT

(cognitive deficits induced by phencyclidine were improved by fluvoxamine but not by paroxetine in mouse)

IT Schizophrenia

(sigma-I receptor agonist such as fluvoxamine would be potential therapeutic drug for treatment of cognitive deficits of schizophrenia)

77-10-1, Phencyclidine
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biólogical study)

(cognitive deficits induced by phencyclidine were improved by fluvoxamine but not by paroxetine in mouse)

IT 54739-18-3, Fluvoxamine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(cognitive deficits induced by phencyclidine were improved by fluvoxamine in mouse)

IT 61869-08-7, Paroxetine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(cognitive deficits induced by phencyclidine were not improved paroxetine in mouse)

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146:493247 CA <<LOGINID::20070611>>

Perospirone augmentation of paroxetine in treatment of refractory TI obsessive-compulsive disorder with depression

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ΑU Otsuka, Tatsui; Togo, Takashi; Sugiyama, Naoya; Uehara, Kumi; Yoshimi, Asuka; Karashima, Aya; Shioya, Hiromi; Hirayasu, Yoshio

Department of Psychiatry, Yokohama City University School of Medicine, Kanazawa-ku, Yokohama, 236-0004, Japan Progress in Neuro-Psychopharmacology & Biological Psychiatry (2007), 31(2), 564-566
CODEN: PNPPD7; ISSN: 0278-5846 S0

PΒ Elsevier B.V.

DT Journal LA English

- 10799320srch2.trn 1-11 (Pharmacology) CC Obsessive-compulsive disorder (OCD) is often complicated by depression. AB We report on a patient with treatment-refractory OCD and treatment-refractory major depression who demonstrated a robust response to augmentation of paroxetine with perospirone. Perospirone is a second-generation antipsychotic agent with antagonist effects on both serotonin 5-HT2A and dopamine D2 receptors, as well as a unique agonist effects on serotonin 5-HT1A receptors. Future studies would be valuable to elucidate the utility of augmentation therapy of selective serotonin reuptake inhibitors with perospirone in the treatment of refractory OCD with depression. perospirone paroxetine obsessive compulsive disorder depression ST antidepressant IT Mental and behavioral disorders (depression; perospirone augmentation of paroxetine was useful and well tolerated in treatment of patient with refractory obsessive-compulsive disorder and depression) IT Mental and behavioral disorders (obsession-compulsion; perospirone augmentation of paroxetine was useful and well tolerated in treatment of patient with refractory obsessive-compulsive disorder and depression) IT Human (perospirone augmentation of paroxetine was useful and well tolerated in patient with refractory obsessive-compulsive disorder and depression possibly due to agonist effect on 5-HT1A in addn. to its antagonist effect on 5-HT2A) **Antidepressants** IT (perospirone augmentation of paroxetine was useful and well tolerated in treatment of patient with refractory obsessive-compulsive disorder and depression) IT 5-HT receptors RL: BSU (Biological study, unclassified); BIOL (Biological study) (type 5-HT1A; perospirone augmentation of paroxetine was useful and well tolerated in patient with refractory obsessive-compulsive disorder and depression possibly due to agonist effect on 5-HT1A in addn. to its antagonist effect on 5-HT2A) 150915-41-6, Perospirone IT RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (perospirone augmentation of paroxetine was useful and well tolerated in patient with refractory obsessive-compulsive disorder and depression possibly due to agonist effect on 5-HT1A in addn. to its antagonist effect on 5-HT2A) 61869-08-7, Paroxetine IT RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (perospirone augmentation of paroxetine was useful and well tolerated in treatment of patient with refractory obsessive-compulsive disorder and depression) RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD (1) Appelberg, B; J Clin Psychiatry 2001, V62, P448 CAPLUS (1) Appelberg, B; J Clin Psychiatry 2001, V62, P448 CAPLUS
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- 146:493155 CA <<LOGINID::20070611>>
- TI
- ΑU
- An analysis on drug use in 530 patients of old age with psycopathy Zhao, Genxiang; Zhang, Jianming Shanghai Mental Health Center, Shanghai, 200030, Peop. Rep. China Shanghai Yiyao (2005), 26(5), 220-223 CODEN: SYHIBK; ISSN: 1006-1533 CS
- SO
- PB Shanghai Yiyao Zazhishe
- DT Journal
- Chinese LA
- 1-11 (Pharmacology) CC
- The drug use in patients of old age with psychopathy are investigated. AB All the records of drug use in patients older than 60 on June 26 2004 were investigated. Frequencies of psychotropic drugs, nootropic drugs, vascular drugs, and cerebral-vascular drugs, DDDs and ranks by expense changed significantly over past. DUIs for most drugs were lower than 1.0 or close 1.0. There were 108 drug combinations. Drugs usages in the patients with psychopathy in our hospital were rational.
- psycopathy old age patient drug use ST
- Natural products, pharmaceutical
 - (Salviae miltiorrhizae radix; anal. on drug use in 530 patients of old age with psycopathy)
- Alzheimer's disease IT
 - Ginkgo
 - Mental and behavioral disorders
 - Moschus
 - Schizophrenia
 - (anal. on drug use in 530 patients of old age with psycopathy)
- Mental and behavioral disorders IT
 - (dementia, vascular; anal. on drug use in 530 patients of old age with psycopathy)
- Mental and behavioral disorders IT
 - (mood-affecting; anal. on drug use in 530 patients of old age with
- psycopathy)
- 50-06-6, Phenobarbital, biological studies IT 50-48-6, Amitriptyline 50-53-3, Chlorpromazine, biological studies 51-68-3, Meclofenoxate 59-92-7, Levodopa, 58-39-9, Chlorperphenazine 52-86-8, Haloperidol
- - 322-35-0, Benserazide 846-49-1, Lorazepam
 - 5786-21-0, Clozapine

 - 17617-23-1, Flurazepam Dlam 29975-16-4, Estazolam 61869-08-
- 79617-96-102518-79-
 - 82626-48-0, Zolpidem 86541-75-5, Benazepril 102 106266-06-2, Risperidone 111974-72-2, Quetiapine 6, Huperzine A
 - 845799-62-4, Notoginseng

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (anal. on drug use in 530 patients of old age with psycopathy)

REFERENCE 10

ΑN 146:492519 CA <<LOGINID::20070611>>

- Effect of Itraconazole on Pharmacokinetics of Paroxetine: the Role of Gut TI Transporters
- Yasui-Furukori, Norio; Saito, Manabu; Niioka, Takenori; Inoue, Yoshimasa; ΑU Sato, Yasushi; Kaneko, Sunao
- Dept. of Neuropsychiatry Hirosaki, University School of Medicine, CS Hirosaki, Japan
- Therapeutic Drug Monitoring (2007), 29(1), 45-48 CODEN: TDMODV; ISSN: 0163-4356 Lippincott Williams & Wilkins S₀
- PB
- Journal DT
- English LA
- 1-Ž (Pharmacology) CC
- AB A recent in vitro study has shown that paroxetine is a substrate of P-glycoprotein. However, there was no in vivo information indicating the involvement of P-glycoprotein on the pharmacokinetics of paroxetine. aim of this study was to examine the effects of itraconazole, a P-glycoprotein inhibitor, on the pharmacokinetics of paroxetine. Two 6 day courses of either 200 mg itraconazole daily or placebo with at least a 4 wk washout period were conducted. Thirteen volunteers took a single oral 20 mg dose of paroxetine on day 6 of both courses. Plasma concns. of paroxetine were monitored up to 48 h after the dosing. Compared with placebo, itraconazole treatment significantly increased the peak plasma concn. (Cmax) of paroxetine by 1.3 fold (6.7 .+-. 2.5 vs. 9.0 .+-. 3.3 ng/mL, P < 0.05) and the area under the plasma concn.-time curve from zero to 48 h [AUC (0-48)] of paroxetine by 1.5 fold (137 .+-. 73 vs. 199 .+-. 91 ng*h/mL, P < 0.01). Although elimination half-life differed significantly (16.1 .+-. 3.4 vs. 18.8 .+-. 5.9 h, P < 0.05), the alteration was small (1.1 fold). The present study demonstrated that the bioavailability of paroxetine was increased by itraconazole, suggesting a possible involvement of P-glycoprotein in the pharmacokinetics of
- itraconazole paroxetine pharmacokinetics bioavailability P glycoprotein ST TT Pharmacokinetics

(higher Cmax, AUC and longer elimination half-life but no change in Tmax of paroxetine was seen with itraconazole treatment in healthy Japanese subject)

IT Drug bioavailability

Drug interactions

Human

Human groups

(increased bioavailability of paroxetine with itraconazole treatment in healthy Japanese subject suggested possible involvement of P-glycoprotein in pharmacokinetics of paroxetine)

IT P-alycoproteins

RL: BSU (Biological study, unclassified); BIOL (Biological study) (increased bioavailability of paroxetine with itraconazole treatment in healthy Japanese subject suggested possible involvement of P-glycoprotein in pharmacokinetics of paroxetine)

61869-08-7, Paroxetine IT

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (increased bioavailability of paroxetine with itraconazole treatment in healthy Japanese subject suggested possible involvement of P-glycoprotein in pharmacokinetics of paroxetine)

84625-61-6, Itraconazole IT

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL Page 21

10799320srch2.trn (Biological study); USES (Uses) (increased bioavailability of paroxetine with itraconazole treatment in healthy Japanese subject suggested possible involvement of P-glycoprotein in pharmacokinetics of paroxetine) RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD (1) Ayrton, A; Xenobiotica 2001, V31, P469 CAPLUS (2) Bertelsen, K; Drug Metab Dispos 2003, V31, P289 CAPLUS (3) Borgers, M; Curr Drug Targets 2005, V6, P849 CAPLUS (4) Fromm, M; Eur J Clin Invest 2003, V33(Suppl 2), P6 (5) Fromm, M; Int J Clin Pharmacol Ther 2000, V38, P69 CAPLUS (6) Furukori, H; Psychopharmacology 1999, V145, P189 CAPLUS (7) Gunasekara, N; Drugs 1998, V55, P85 CAPLUS (7) Gunasekara, N; Drugs 1998, V55, P85 CAPLUS
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CC 1-6 (Pharmacology)

TI Cytotoxicity of different selective serotonin reuptake inhibitors (SSRIs) against cancer cells

ST paroxetine venlafaxine antitumor non small cell lung cancer

IT Cell death

(cell death was caused by paroxetine in human non small cell lung Page 23

```
10799320srch2.trn
          cancer, non cancerous fibroblast and murine cell lines)
IT
      Lung, neoplasm
          (non-small-cell carcinoma; paroxetine but not venlafaxine possessed cytotoxic activity against tumor in human non small cell lung cancer,
          non cancerous fibroblast and murine cell lines)
IT
      Antitumor agents
      Human
          (paroxetine but not venlafaxine possessed cytotoxic activity against
          tumor in human non small cell lung cancer, non cancerous fibroblast and
          murine cell lines)
IT
         (pulmonary non-small-cell; paroxetine but not venlafaxine possessed cytotoxic activity against tumor in human non small cell lung cancer,
          non cancerous fibroblast and murine cell lines)
IT
      5-HT reuptake inhibitors
          (selective serotonin reuptake inhibitor paroxetine but not venlafaxine
        possessed cytotoxic activity against tumor in human non small cell lung cancer, non cancerous fibroblast and murine cell lines)
***61869-08-7***, Paroxetine
                                , Paroxetine
IT
      RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
      (Biological study); USES (Uses)
          (paroxetine possessed cytotoxic activity against tumor in human non
          small cell lung cancer, non cancerous fibroblast and murine cell lines)
      93413-69-5, Venlafaxine
IT
      RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
      (Biological study); USES (Uses)

(venlafaxine did not possess cytotoxic activity against tumor in human non small cell lung cancer, non cancerous fibroblast and murine cell
          lines)
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end
=> s l1/prep
            2346 L1
         4415211 PREP/RL
L3
               91 L1/PREP
                     (L1 (L) PREP/RL)
=> d scan
L3 ·
                       CAPLUS COPYRIGHT 2007 ACS on STN
       91 ANSWERS
      27-16 (Heterocyclic Compounds (One Hetero Atom))
CC
TI.
      Rhodium-Catalyzed Asymmetric 1,4-Addition of Organoboron Reagents to
      5,6-Dihydro-2(1H)-pyridinones. Asymmetric Synthesis of
      4-Aryl-2-piperidinones
      asym synthesis arylpiperidinone; stereoselective addn organoboron pyridinone; paroxetine intermediate stereoselective prepn
ST
      Asymmetric synthesis and induction
TT
          (rhodium-catalyzed asym. 1,4-addn. of organoboron reagents to
          5,6-dihydro-2(1H)-pyridinones)
IT
      Addition reaction
      Addition reaction catalysts
          (stereoselective; rhodium-catalyzed asym. 1,4-addn. of organoboron reagents to 5,6-dihydro-2(1H)-pyridinones)
      12082-47-2 76189-55-4, (R)-BINAP 139139-86-9 256393-29-0 RL: CAT (Catalyst use); USES (Uses) (rhodium-catalyzed asym. 1,4-addn. of organoboron reagents to
IT
          5,6-dihydro-2(1H)-pyridinones)
      355392-45-9P
IT
      RL: CAT (Catalyst use): SPN (Synthetic preparation): PREP (Preparation):
      USES (Uses)
          (rhodium-catalyzed asym. 1,4-addn. of organoboron reagents to
          5,6-dihydro-2(1H)-pyridinones)
                                                Page 24
```

```
10799320srch2.trn
                              , (-)-Paroxetine
        ***61869-08-7P***
IT
                                                    ***PREP (Preparation)***
      RL: PNU (Preparation, unclassified);
         (rhodium-catalyzed asym. 1,4-addn. of organoboron reagents to
         5,6-dihydro-2(1H)-pyridinones)
      98-80-6, Phenylboronic acid 1679-18-1, 4-Chlorophenylboronic acid 1765-93-1, 4-Fluorophenylboronic acid 14804-38-7, 1-Bromo-4-methoxy-3,5-
IT
                           126613-06-7
                                            128773-72-8
      dimethylbenzene
      RL: RCT (Reactant); RACT (Reactant or reagent)
          (rhodium-catalyzed asym. 1,4-addn. of organoboron reagents to
         5,6-dihydro-2(1H)-pyridinones)
      448-59-9P, Tris(4-Fluorophenyl)boroxin 7519-91-7P, Tris(4-chlorophenyl)boroxin
                                                       3262-89-3P, Triphenylboroxin
IT
                                                      122708-97-8P
                                                                          125653-55-6P
      377076-16-9P
      RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
      (Reactant or reagent)
         (rhodium-catalyzed asym. 1,4-addn. of organoboron reagents to 5,6-dihydro-2(1H)-pyridinones)
      177966-76-6P
IT
                                                                              377076-15-8P
     RL: SPN (Synthetic preparation); PREP (Preparation) (rhodium-catalyzed asym. 1,4-addn. of organoboron reagents to
         5,6-dihydro-2(1H)-pyridinones)
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end
=> d 12 4 ibib abs
L2 ANSWER 4 OF 2346 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2007:538588 CAPLUS <<LOGINID::20070611>>
DOCUMENT NUMBER:
                              146:501032
TITLE:
                              Process for preparing paroxetine hydrochloride
                              hemihydrate
                              Dubey, Shailendra Kumar; Kumar, Pramod; Dubey, Sushil
INVENTOR(S):
                              Kumar
PATENT ASSIGNEE(S):
                              Jubilant Organosys Ltd., India
                              PCT Int. Appl., 17pp.
SOURCE:
                              CODEN: PIXXD2
DOCUMENT TYPE:
                              Patent
LANGUAGE:
                              English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
                                                    APPLICATION NO.
      PATENT NO.
                              KIND
                                      DATE
                                                                                DATE
     wo 2007054978
                              Α2
                                      20070518
                                                    WO 2006-IN446
                                                                                20061110
               MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO,
               RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT,
               TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
          RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.:
                                                    IN 2005-DE3007
                                                                            A 20051110
      A process for the prepn. of cryst. paroxetine hydrochloride in hemihydrate
      form employing a selective solvent system to achieve stable and
      non-hygroscopic form which is easy to prep. and convenient to operate on
      com. scale is described. The process comprises crystg. paroxetine
      hydrochloride using an alc. solvent, such as methanol, ethanol,
```

Page 25

n-propanol, isopropanol or their mixt. and isolating the crystd. product by optionally adding secondary solvent, such as diisopropyl ether or Me tert-Bu ether.

=> file registrygistry
'REGISTRYGIST' IS NOT A VALID FILE NAME
SESSION CONTINUES IN FILE 'CAPLUS'
Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files
that are available. If you have requested multiple files, you can
specify a corrected file name or you can enter "IGNORE" to continue
accessing the remaining file names entered.

=> file registry COST IN U.S. DOLLARS SINCE FILE TOTAL **ENTRY SESSION** 11.89 FULL ESTIMATED COST 31.48 DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE **TOTAL ENTRY SESSION** CA SUBSCRIBER PRICE -0.78-1.51

FILE 'REGISTRY' ENTERED AT 15:57:20 ON 11 JUN 2007 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2007 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 10 JUN 2007 HIGHEST RN 936909-28-3 DICTIONARY FILE UPDATES: 10 JUN 2007 HIGHEST RN 936909-28-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> cost
COST IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> d cost		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
CONNECT CHARGES	6.24	16.41
NETWORK CHARGES	0.96	2.70
SEARCH CHARGES	0.00	6.96
DISPLAY CHARGES	0.00	12.61
FULL ESTIMATED COST	7.20	38.68

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE TOTAL ENTRY SESSION

CA SUBSCRIBER PRICE

0.00 -1.51

IN FILE 'REGISTRY' AT 16:07:03 ON 11 JUN 2007

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS SINCE FILE **TOTAL ENTRY SESSION** FULL ESTIMATED COST 18.45 49.93 DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE **TOTAL ENTRY** SESSION CA SUBSCRIBER PRICE 0.00 -1.51

STN INTERNATIONAL LOGOFF AT 16:22:12 ON 11 JUN 2007